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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,796	03/15/2001	Timothy J. Jegla	018512-005010US	6783

20350 7590 10/20/2004

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/20/2004

Remail

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/810,796	JEGLA, TIMOTHY J.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16, 18* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 10 June 2003 (Paper No. 17) has been entered in full.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 41-48 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the specification at pg 3 of the previous Office Action (Paper No. 15, 12 March 2003) is *withdrawn* in view of the deleted hyperlink in the specification (Paper No. 17, 10 June 2003).

2. The supplemental information disclosure statements filed on 20 May 2003 (Paper No. 16) and 10 June 2003 (Paper No. 18) have been considered.

Claim Rejections - 35 USC § 112

3. Claims 41-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding a polypeptide comprising an alpha subunit of a KCNQ potassium channel, wherein said polypeptide forms, with at least one additional KCNQ alpha subunit, a KCNQ potassium channel having the characteristic of voltage-gating; and wherein said nucleic acid specifically hybridizes under stringent conditions to the nucleic acid of SEQ ID NOs: 1, 2, or 3 and that encodes an amino acid sequence of SEQ ID NO: 4 or 5, wherein the hybridization reaction is incubated at 42°C in a solution comprising 50% formamide, 5x SSC, and 1% SDS and washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS, does not reasonably provide enablement for an isolated nucleic acid encoding a

polypeptide comprising an alpha subunit of a KCNQ potassium channel, wherein said polypeptide forms, with at least one additional KCNQ alpha subunit, a KCNQ potassium channel having the characteristic of voltage-gating; and wherein said nucleic acid specifically hybridizes under stringent conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO: 4 or 5, wherein the hybridization reaction is incubated at 42°C in a solution comprising 50% formamide, 5x SSC, and 1% SDS and washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth for claims 41-48 at pg 3-7 of the previous Office Action (Paper No. 15, 12 March 2003).

The claims also recite an expression vector comprising the nucleic acid and a host cell transfected with the vector. The claims recite that the polypeptide encoded by the nucleic acid comprises an alpha subunit of a homomeric or heterimeric potassium channel.

Applicant's arguments (Paper No. 17, 10 June 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that working examples of human KCNQ coding sequence and amino acid sequence are provided. Applicant states that the specification also contains ample directions to practice the invention, such as methods of cloning KCNQ nucleic acid sequences (pg 26-29), expression of KCNQ nucleic acid sequences (pg 29-31), purifications of KCNQ polypeptides (pg 31-34), immunological detection of KCNQ polypeptides (pg 34-41), and assays for modulators of KCNQ (pg 41-48). Applicant argues that the KCNQ potassium channel variants can be readily tested according to the methods commonly used by those skilled in the art or the methods

taught by the specification to eliminate inoperable embodiments. Applicant contends that although some experimentation may be involved to practice the claimed invention, such experimentation utilizes well-established techniques and is the type routinely conducted in the art. Applicant states that the experimentation does not constitute undue experimentation.

Applicant's arguments have been fully considered but are not found to be persuasive. Furthermore, although the specification in the instant application teaches art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active KCNQ derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The skilled artisan must resort to trial and error experimentation to generate the infinite number of variants and fragments of KCNQ polynucleotides and polypeptides, as recited in the claims and to screen them for a desired activity (e.g., forming a KCNQ potassium channel with at least one additional KCNQ alpha subunit). Such trial and error is considered undue.

Additionally, the broad brush discussion of making and screening for KCNQ variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the KCNQ nucleic acid sequences of SEQ ID NOs: 1, 2, and 3 and the amino acid sequences of SEQ ID NOs: 4 and 5 are disclosed. It is noted that the nucleic acid sequences of SEQ ID NOs: 2 and 3 are closely related in that a 27 nucleotide segment present in SEQ ID NO: 2 is absent from SEQ ID NO: 3 (pg 59, lines 27-32; specification). The nucleic acid sequence of SEQ ID NO: 1 is the full-length sequence of SEQ ID NO: 2. Furthermore, regarding the amino acid sequences of SEQ ID NOs: 4 and 5, in one particular region of SEQ ID NO: 5, there is one different amino acid and adjacent to this, 9 other

amino acids are missing that are present in SEQ ID NO: 4 (Figure 1). Therefore, the specification of the instant application is only teaching two forms of the same protein and the specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error.

The Examiner acknowledges that it is not a function of the claims to specifically exclude possible inoperative embodiments, and the presence of inoperative embodiments within the scope of a claim does not preclude enablement of the claim. However, the scope of the claim may still not be enabled where undue experimentation is involved in determining those embodiments that are operable. MPEP § 2164.08(b) states that "claims reading on significant numbers of inoperative embodiments would render the claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.

(ii) Applicant asserts that one need not disclose all possible embodiments to meet the enablement requirement. Applicant argues that the claimed nucleic acids are defined, in addition to a sequence-based structural feature, by a functional feature: the ability to form a voltage-gated KCNQ potassium channel with at least one other KCNQ alpha subunit. Applicant submits that this functional feature is testable by an ordinary skilled artisan according to the methods known in the art or taught by the disclosure (pg 41-48).

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, according to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of

experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis". As mentioned above, the skilled artisan must resort to trial and error experimentation to generate the infinite number of variants and fragments of KCNQ polynucleotides and polypeptides, as recited in the claims and to screen them for a desired activity (e.g., forming a KCNQ potassium channel with at least one additional KCNQ alpha subunit). Such trial and error is considered undue.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which fail to recite particular biological activities and also embrace a broad class of structural variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

4. Claims 41-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. The basis for this rejection is set forth for claims 41-48 at pg 7-9 of the previous Office Action (Paper No. 15, 12 March 2003).

Specifically, the claims are directed to an isolated nucleic acid encoding a polypeptide comprising an alpha subunit of a KCNQ potassium channel, wherein said polypeptide forms, with at least one additional KCNQ alpha subunit, a KCNQ potassium channel having the characteristic of voltage-gating; and wherein said nucleic acid specifically hybridizes under stringent conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO: 4 or 5, wherein the hybridization reaction is incubated at 42°C in a solution comprising 50% formamide, 5x SSC, and 1% SDS and washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS. The claims also recite an expression vector comprising the nucleic acid and a host cell transfected with the vector. The claims recite that the polypeptide encoded by the nucleic acid comprises an alpha subunit of a homomeric or heterimeric potassium channel.

Applicant's arguments (Paper No. 17, 10 June 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the pending claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Circ. 1997). Applicant submits that proper description of functional features of a claimed invention can play an important role in satisfying the written description requirement. It is noted that Applicant cites *Amgen Inc. V. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003). Applicant argues that with regard to the claimed nucleic acids, claim 41 sets forth both functional features, e.g. encoding a polypeptide comprising an alpha subunit of a KCNQ potassium channel, which polypeptide forms, with at least one

additional KCNQ alpha subunit, a voltage-gated KCNQ potassium channel, and structural features, e.g., capable of hybridizing to a nucleic acid encoding an amino acid sequence of SEQ ID NO: 5 under specified hybridization conditions. Applicant argues that the ability for a nucleic acid to hybridize under given conditions to a reference polynucleotide sequence is a particular/structural property of the nucleic acid, because it relies upon the nucleotide sequence of the molecule. Applicant also contends that the functional features of the claimed nucleic acids can be readily tested by one of ordinary skill in the art using well established, routinely practiced techniques as well as according to the teaching of the present specification.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polynucleotides recited in the claims. The scope of the claims include numerous structural variants. The specification's discussion of screening the structural variants for the functional activity of encoding a polypeptide comprising an alpha subunit of a KCNQ potassium channel, which polypeptide forms, with at least one additional KCNQ alpha subunit, a voltage-gated KCNQ potassium channel, constitutes an invitation of the skilled artisan to experiment by trial and error. Although the specification discloses the structure and function of the KCNQ polypeptide of SEQ ID NOs: 4 and 5, this description is not a representative number to support the description of an entire genus of functionally equivalent KCNQ polynucleotides which encode the polypeptide of SEQ ID NOs: 4 or 5. It is noted that the nucleic acid sequences of SEQ ID NOs: 2 and 3 are closely related in that a 27 nucleotide segment present in SEQ ID NO: 2 is absent from SEQ ID NO: 3 (pg 59, lines 27-32; specification). The nucleic acid sequence of SEQ ID NO: 1 is the full-length

sequence of SEQ ID NO: 2. Furthermore, regarding the amino acid sequences of SEQ ID NOs: 4 and 5, in one particular region of SEQ ID NO: 5, there is one different amino acid and adjacent to this, 9 other amino acids are missing that are present in SEQ ID NO: 4 (Figure 1). The specification of the instant application is only teaching two forms of the same protein. Therefore, only an isolated nucleic acid molecule encoding a polypeptide comprising an alpha subunit of a KCNQ potassium channel, wherein said polypeptide forms, with at least one additional KCNQ alpha subunit, a KCNQ potassium channel having the characteristic of voltage-gating; and wherein said nucleic acid specifically hybridizes under stringent conditions to the nucleic acid of SEQ ID NOs: 1, 2, or 3 and that encodes an amino acid sequence of SEQ ID NO: 4 or 5, wherein the hybridization reaction is incubated at 42°C in a solution comprising 50% formamide, 5x SSC, and 1% SDS and washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Furthermore, the broad brush discussion of making or screening for variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only one member, the nucleic acid molecule of SEQ ID NOs: 1, 2, or 3 that encode the amino acid sequence of SEQ ID NO: 4 or 5, was disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

Additionally, with regard to claims 41-48, simply reciting hybridization conditions in the claims does not yield adequate written description of the polynucleotides encompassed. The

claims encompass an infinite number of polynucleotides that hybridize to a nucleic acid encoding an amino acid sequence of SEQ ID NO: 5. These polynucleotides may be structurally and functionally divergent from the polynucleotides of SEQ ID NOs: 1, 2, or 3.

(ii) Applicant disagrees with the Examiner's reading of *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 and application of *Fiddes* in the present case. Applicant argues that the fact pattern of *Fiddes* in not analogous to that of the present case. Applicant states that the patent applicants in *Fiddes* sought to patent a large genus of polypeptides and polynucleotides when they did not have in their possession any correct polynucleotide sequence. Applicant indicates that the Board's finding of inadequate written description was based on the notion that the claim of a genus of polynucleotides cannot be adequately supported when only an inaccurate polynucleotide sequence was disclosed. Applicant contends that in contrast to *Fiddes*, Applicant has in his possession both the amino acid sequences of two KCNQ potassium channel subunits (SEQ ID NOs: 2 and 3) and the naturally occurring nucleotide sequences encoding the subunits (SEQ ID NOs: 4 and 5). Applicant also argues that the claims are not drawn to a broad genus of molecules without specific structural or functional definition. Applicant submits that both structural and functional features commonly shared by all members of the claimed genus have been described in detail.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the fact pattern of *Fiddes* is analogous to that of the present case. In *Fiddes,* the claims directed to the broad class of mammalian FGF's did not have adequate written description since the patent only teaches the amino acid sequence for bovine pituitary FGF and the

theoretical DNA sequence encoding that factor. Knowledge of the amino acid sequence of the protein, along with the state of the art that establishes the degeneracy of the genetic code, does not establish the inventor's possession of the gene encoding the protein. In the instant application, the claims are drawn to a broad genus of nucleic acid molecules. The specification does not provide adequate written description for all nucleic acid degenerates that encode the amino acid sequences of SEQ ID NO: 4 or 5 and wherein the polypeptide forms with at least one other KCNQ alpha subunit, a potassium channel that has the characteristic of voltage-gating. As mentioned above, the nucleic acid sequences of SEQ ID NOs: 2 and 3 are closely related in that a 27 nucleotide segment present in SEQ ID NO: 2 is absent from SEQ ID NO: 3 (pg 59, lines 27-32; specification). The nucleic acid sequence of SEQ ID NO: 1 is the full-length sequence of SEQ ID NO: 2. Furthermore, regarding the amino acid sequences of SEQ ID NOs: 4 and 5, in one particular region of SEQ ID NO: 5, there is one different amino acid and adjacent to this, 9 other amino acids are missing that are present in SEQ ID NO: 4 (Figure 1). Therefore, the specification of the instant application is only teaching two forms of the same protein. The claims of the instant application are also broad in that they are not limited to only mammalian nucleic acid sequences (for example), but encompass other classes such as insects, birds, bacteria, reptiles, etc.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
20 August 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER